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FIG. 1A

TCTAGATCTA GCTGGTGTGT CTCTGATCTT GCTTCTTTTC TCCCAGCCCT 50

TCCTACTTGT GTGAGAACAA GGTTTTGAGC CATGGAGCAA AGAGGTTGGA 100

CTCTGCAGTG TACTGCTTTC GCCTTCTTTT GCGTTTGGTG TGCACTAAGC 150

AGTGTAAGAG CAAAGAGGCA GTTTGTTAAT GAATGGGCGG CGGAGATCCC 200

CGGAGGGCAA GAAGCTGCCT CTGCCATCGC CGAAGAAGTG GGGTATGACC 250

TTTTGGGTCA GATTGGATCA CTTGAAAATC ACTATTTATT CAAACACAAA 300

AGCCATCCTC GGAGGTCCCG AAGAAGCGCT CTTCATATCA CTAAGAGGTT 350

ATCTGATGAT GATCGTGTGA CGTGGGCTGA ACAACAGTAT GAAAAAGAGA 400

GAAGTAAACG TTCAGTTCAA AAAGACTCAG CATTGGATCT CTTCAATGAT 450

CCAATGTGGA ATCAGCAGTG GTACTTGCAA GATACCAGAA TGACTGCAGC 500

TCTGCCCAAG CTGGACCTTC ATGTAATACC TGTTTGGGAA AAGGGTATTA 550

CTGGCAAAGG AGTTGTTATT ACTGTACTGG ATGATGGCTT GGAGTGGAAT 600

CACACAGACA TTTATGCCAA TTATGATCCA GAGGCTAGCT ATGATTTTAA 650

CGATAATGAT CATGATCCAT TTCCCCGATA TGATCTCACA AATGAAAACA 700

AACATGGAAC AAGATGTGCA GGTGAAATTG CCATGCAAGC AAATAATCAC 750

AAGTGTGGGG TTGGAGTTGC ATATAATTCC AAAGTTGGAG GCATAAGAAT 800

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FIG. 1B

GCTGGATGGC ATTGTAAGTG ATGCCATTGA GGCTAGTTCA ATTGGATTCA 850
ACCCTGGCCA TGTGGATATT TACAGTGCAA GCTGGGGCCC TAATGATGAT 900
GGAAAACTG TGGAGGGGCC TGGCAGACTA GCCCAGAAGG CATTGAATA 950
TGGTGTCAAA CAGGGGAGAC AAGGGAAAGG CTCCATCTTT GTCTGGGCTT 1000
CAGGGAATGG GGGTCGTCAG GGAGATAACT GTGACTGTGA TGGCTACACA 1050
GACAGCATTT ACACCATCTC TATCAGCAGT GCCTCCCAGC AAGGCCTGTC 1100
ACCTTGGTAT GCAGAGAAGT GTTCTTCCAC ATTGGCTACC TCCTACAGCA 1150
GTGGTGATTA CACAGACCAG CGAATAACAA GCGCTGACCT GCACAATGAC 1200
TGCACAGAGA CCCACACAGG CACCTCGGCT TCAGCACCCC TGGCTGCTGG 1250
TATCTTTGCT CTGGCCTTGG AGGCAAACCC AAATCTTACC TGGAGAGATA 1300
TGCAGCATCT GGTGTCTGAG ACCTCTGAGT ACGACCCATT GGCCAGTAAC 1350
CCAGGTTGGA AAAAGAATGG GGCAGGCTTG ATGGTGAACA GCCGATTG 1400
ATTTGGCTTG CTAAATGCCA AAGCTCTGGT GGATTGCTG GATCCTCGGA 1450
CCTGGAGAAA TGTGCCTGAG AAGAAAGAAT GTGTTGTAAA AGACAATAAC 1500
TTTGAGCCTA GAGCCCTGAA AGCTAATGGA GAAGTAATTG TTGAAATCCC 1550
AACAAGAGCT TGTGAAGGAC AAGAAAATGC TATCAAGTCT CTGGAACATG 1600
TGCAATTTGA AGCAACAATT GAATATTCTC GTAGAGGAGA CCTTCATGTC 1650

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FIG. 1C

ACACTCACTT CTGCTGTTGG AACCAGCACT GTACTGTTGG CTGAAAGGGA 1700

AAGAGATACA TCCCCCAATG GCTTTAAGAA TTGGGACTTC ATGTCTGTTT 1750

ATACATGGGG AGAGAATCCT GTAGGCACCT GGACATTGAA AATTACAGAC 1800

ATGTCTGGAA GAATGCAAAA TGAAGGAAGG ATTGTGAACT GGAAGTTGAT 1850

TTTGCATGGG ACATCTTCTC AACCAGAGCA CATGAAGCAG CCCCCTGTGT 1900

ACACATCCTA CAATACAGTC CAGAATGACA GGAGAGGAGT GGAAAAGATG 1950

CCTGGTACCC AAAAATCCA GCAGCAGCAA TGTGGAGGGT AGAAGGGATG 2050

AGCAGGTACA AGGAACTCCT TCAAAGGCCA TGCTGCGACT CCTACAAAGT 2100

GCTTTTAGCA AGAATGCACT TTCAAACAA TCACCAAAGA AGTCTCCAAG 2150

TGCAAAGCTC AGCATCCCTT ATGAAAGTTT CTATGAAGCC TTGGAAAAGC 2200

TTAACAAGCC CTCCAAGCTT GAAGGCTCTG AAGACAGTCT GTACAGTGAC 2250

TATGTTGATG TATTCTATAA CACAAAACCT TATAAGCATA GAGATGACAG 2300

GCTGCTGCAA GCTCTCATGG ACATCCTAAA TGAGGAGAAT TAAAATAAGG 2350

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FIG. 2A

TCTAGATGCA TCTTCCCTCT TCGTCCCCTG CTCCACCACC CTGCGCGCCT 50
CACAGCCCCG CTTTTCAC TC CAAAGAAGG ATGGAGGGCG GTTGTGGATC 100
CCAGTGAAG GCGGCCGGGT TCCTCTTCTG TGTGATGGTT TTTGCGTCTG 150
CCGAGAGACC CGTCTTCACG AATCATTTTC TTGTGGAGTT GCATAAAGAC 200
GGAGAGGAAG AGGCTCGCCA AGTTGCAGCA GAACACGGCT TTGGAGTCCG 250
AAAGCTCCCC TTGTCAGAAG GCCTGTATCA CTTTATCAC AATGGGCTTG 300
CAAAGGCCAA AAGAAGACGC AGCCTACACC ATAAGCGGCA GCTAGAGAGA 350
GACCCAGGA TAAAGATGGC GCTGCAACAA GAAGGATTTG ACCGTAAAAA 400
GAGAGGGTAC AGGGACATCA ATGAGATTGA CATCAACATG AATGATCCTC 450
TCTTTACAAA GCAATGGTAC CTGTTCAACA CTGGGCAAGC CGATGGAAC 500
CCTGGGCTAG ACTTGAACGT GGCCGAAGCC TGGGAGCTGG GATACACAGG 550
AAAAGGAGTG ACCATTGGAA TTATGGATGA TGAATTGAC TATCTCCACC 600
CAGACCTGGC CTACAACTAC AACGCTGATG CAAGTTATGA CTCAGCAGC 650
AATGACCCCT ACCCATACCC TCGATACACA GATGACTGGT TCAACAGCCA 700
TGGAAGTAGG TGTGCAGGAG AAGTTTCTGC TGCAGCCAGC AACAATATCT 750
GTGGAGTCGG CGTAGCATAC AACTCCAAGG TGGCAGGGAT CCGGATGCTG 800
GACCAGCCCT TTATGACAGA CATCATCGAA GCCTCCTCCA TCAGCCACAT 850

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FIG. 2B

GCCTCAACTG ATCGACATCT ACAGTGCAAG CTGGGGCCCC ACAGACAATG 900

GGAAGACGGT TGATGGGCCC CGAGAGCTCA CACTCCAGGC CATGGCTGAT 950

GGCGTGAACA AGGGCCGTGG GGGCAAAGGC AGCATCTATG TGTGGGCCTC 1000

TGGGGACGGT GGCAGCTACG ATGACTGCAA CTGTGACGGC TATGCTTCAA 1050

GCATGTGGAC CATCTCCATC AACTCAGCCA TCAATGATGG CAGGACTGCC 1100

TTGTATGATG AGAGTTGCTC TTCCACCTTA GCATCCACCT TCAGCAATGG 1150

GAGGAAGAGG AATCCTGAGG CTGGTGTGGC TACCACAGAC TTGTATGGCA 1200

ACTGTACTCT GAGACACTCT GGGACATCTG CAGCTGCTCC GGAGGCAGCT 1250

GGCGTGTTTG CATTAGCTTT GGAGGCTAAC CTGGATCTGA CCTGGAGAGA 1300

CATGCAACAT CTGACTGTGC TCACCTCCAA GCGGAACCAG CTTCATGATG 1350

AGGTTTCATCA GTGGCGACGG AATGGGGTTG GCCTGGAATT TAATCACCTC 1400

TTTGGCTACG GAGTCCTTGA TGCAGGTGCC ATGGTGAAAA TGGCTAAAGA 1450

CTGGAAACT GTTCCGGAGA GATTCCATTG TGTGGGAGGC TCTGTGCAGA 1500

ACCCTGAAAA AATACCACCC ACCGGCAAGC TGGTACTGAC CCTCAAAACA 1550

AATGCATGTG AGGGGAAGGA AACTTCGTC CGCTACCTGG AGCACGTCCA 1600

AGCTGTCATC ACAGTCAACG CGACCAGGAG AGGAGACCTG AACATCAACA 1650

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FIG. 2C

TGACCTCCCC AATGGGCACC AAGTCCATTT TGCTGAGCCG GCGTCCCAGA 1700
GACGACGACT CCAAGGTGGG CTTTGACAAG TGGCCTTTCA TGACCACCCA 1750
CACCTGGGGG GAGGATGCCC GAGGGACCTG GACCCTGGAG CTGGGGTTTG 1800
TGGCAGTGC ACCACAGAAG GGGTTGCTGA AGGAATGGAC CCTGATGCTT 1850
CACGGCACAC AGAGCGCCCC ATACATCGAT CAGGTGGTGA GGGATTACCA 1900
GTCTAAGCTG GCCATGTCCA AGAAGCAGGA GCTGGAGGAA GAGCTGGATG 1950
AGGCTGTGGA GAGAAAGCCTG CAAAGTATCC TGAGAAAGAA CTAGGGCCAC 2000
GCTTCCGAAT TC 2012

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FIG. 3A

Met	Glu	Gln	Arg	Gly	Trp	Thr	Leu	Gln	Cys	Thr	Ala	Phe	Ala	Phe	1	5	10	15
Phe	Cys	Val	Trp	Cys	Ala	Leu	Ser	Ser	Val	Lys	Ala	Lys	Arg	Gln	20	25	30	
Phe	Val	Asn	Glu	Trp	Ala	Ala	Glu	Ile	Pro	Gly	Gly	Gln	Glu	Ala	35	40	45	
Ala	Ser	Ala	Ile	Ala	Glu	Glu	Leu	Gly	Tyr	Asp	Leu	Leu	Gly	Gln	50	55	60	
Ile	Gly	Ser	Leu	Glu	Asn	His	Tyr	Leu	Phe	Lys	His	Lys	Ser	His	65	70	75	
Pro	Arg	Arg	Ser	Arg	Arg	Ser	Ala	Leu	His	Ile	Thr	Lys	Arg	Leu	80	85	90	
Ser	Asp	Asp	Asp	Arg	Val	Thr	Trp	Ala	Glu	Gln	Gln	Tyr	Glu	Lys	95	100	105	
Glu	Arg	Ser	Lys	Arg	Ser	Val	Gln	Lys	Asp	Ser	Ala	Leu	Asp	Leu	110	115	120	
Phe	Asn	Asp	Pro	Met	Trp	Asn	Gln	Gln	Trp	Tyr	Leu	Gln	Asp	Thr	125	130	135	
Arg	Met	Thr	Ala	Ala	Leu	Pro	Lys	Leu	Asp	Leu	His	Val	Ile	Pro	140	145	150	
Val	Trp	Glu	Lys	Gly	Ile	Thr	Gly	Lys	Gly	Val	Val	Ile	Thr	Val	155	160	165	
Leu	Asp	Asp	Gly	Leu	Glu	Trp	Asn	His	Thr	Asp	Ile	Tyr	Ala	Asn	170	175	180	
Tyr	Asp	Pro	Glu	Ala	Ser	Tyr	Asp	Phe	Asn	Asp	Asn	Asp	His	Asp	185	190	195	
Pro	Phe	Pro	Arg	Tyr	Asp	Leu	Thr	Asn	Glu	Asn	Lys	His	Gly	Thr	200	205	210	
Arg	Cys	Ala	Gly	Glu	Ile	Ala	Met	Gln	Ala	Asn	Asn	His	Lys	Cys	215	220	225	
Gly	Val	Gly	Val	Ala	Tyr	Asn	Ser	Lys	Val	Gly	Gly	Ile	Arg	Met	230	235	240	

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FIG. 3B

Leu Asp Gly Ile	Val Thr Asp Ala Ile	Glu Ala Ser Ser Ile	Gly
245		250	255
Phe Asn Pro Gly	His Val Asp Ile Tyr	Ser Ala Ser Trp Gly	Pro
260		265	270
Asn Asp Asp Gly	Lys Thr Val Glu Gly	Pro Gly Arg Leu Ala	Gln
275		280	285
Lys Ala Phe Glu	Tyr Gly Val Lys Gln	Gly Arg Gln Gly Lys	Gly
290		295	300
Ser Ile Phe Val	Trp Ala Ser Gly Asn	Gly Gly Arg Gln Gly	Asp
305		310	315
Asn Cys Asp Cys	Asp Gly Tyr Thr Asp	Ser Ile Tyr Thr Ile	Ser
320		325	330
Ile Ser Ser Ala	Ser Gln Gln Gly Leu	Ser Pro Trp Tyr Ala	Glu
335		340	345
Lys Cys Ser Ser	Thr Leu Ala Thr Ser	Tyr Ser Ser Gly Asp	Tyr
350		355	360
Thr Asp Gln Arg	Ile Thr Ser Ala Asp	Leu His Asn Asp Cys	Thr
365		370	375
Glu Thr His Thr	Gly Thr Ser Ala Ser	Ala Pro Leu Ala Ala	Gly
380		385	390
Ile Phe Ala Leu	Ala Leu Glu Ala Asn	Pro Asn Leu Thr Trp	Arg
395		400	405
Asp Met Gln His	Leu Val Val Trp Thr	Ser Glu Tyr Asp Pro	Leu
410		415	420
Ala Ser Asn Pro	Gly Trp Lys Lys Asn	Gly Ala Gly Leu Met	Val
425		430	435
Asn Ser Arg Phe	Gly Phe Gly Leu Leu	Asn Ala Lys Ala Leu	Val
440		445	450
Asp Leu Ala Asp	Pro Arg Thr Trp Arg	Asn Val Pro Glu Lys	Lys
455		460	465
Glu Cys Val Val	Lys Asp Asn Asn Phe	Glu Pro Arg Ala Leu	Lys
470		475	480

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FIG. 3C

Ala Asn Gly Glu Val Ile Val Glu Ile	Pro Thr Arg Ala Cys Glu
485	490 495
Gly Gln Glu Asn Ala Ile Lys Ser Leu	Glu His Val Gln Phe Glu
500	505 510
Ala Thr Ile Glu Tyr Ser Arg Arg Gly	Asp Leu His Val Thr Leu
515	520 525
Thr Ser Ala Val Gly Thr Ser Thr Val	Leu Leu Ala Glu Arg Glu
530	535 540
Arg Asp Thr Ser Pro Asn Gly Phe Lys	Asn Trp Asp Phe Met Ser
545	550 555
Val His Thr Trp Gly Glu Asn Pro Val	Gly Thr Trp Thr Leu Lys
560	565 570
Ile Thr Asp Met Ser Gly Arg Met Gln	Asn Glu Gly Arg Ile Val
575	580 585
Asn Trp Lys Leu Ile Leu His Gly Thr	Ser Ser Gln Pro Glu His
590	595 600
Met Lys Gln Pro Arg Val Tyr Thr Ser	Tyr Asn Thr Val Gln Asn
605	610 615
Asp Arg Arg Gly Val Glu Lys Met Val	Asn Val Val Glu Lys Arg
620	625 630
Pro Thr Gln Lys Ser Leu Asn Gly Asn	Leu Leu Val Pro Lys Asn
635	640 645
Ser Ser Ser Ser Asn Val Glu Gly Arg	Arg Asp Glu Gln Val Gln
650	655 660
Gly Thr Pro Ser Lys Ala Met Leu Arg	Leu Leu Gln Ser Ala Phe
665	670 675

Ser Lys Asn Ala	Leu Ser Lys Gln Ser	Pro Lys Lys Ser Pro Ser	
680		685	690
Ala Lys Leu Ser Ile Pro Tyr Glu Ser Phe Tyr Glu Ala Leu Glu		700	705
695			
Lys Leu Asn Lys Pro Ser Lys Leu Glu Gly Ser Glu Asp Ser Leu		715	720
710			
Tyr Ser Asp Tyr Val Asp Val Phe Tyr Asn Thr Lys Pro Tyr Lys		730	735
725			
His Arg Asp Asp Arg Leu Leu Gln Ala Leu Met Asp Ile Leu Asn		745	750
740			
Glu Glu Asn			
753			

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FIG. 4A

Met	Glu	Gly	Gly	Cys	Gly	Ser	Gln	Trp	Lys	Ala	Ala	Gly	Phe	Leu	1	5	10	15
Phe	Cys	Val	Met	Val	Phe	Ala	Ser	Ala	Glu	Arg	Pro	Val	Phe	Thr	20	25	30	
Asn	His	Phe	Leu	Val	Glu	Leu	His	Lys	Asp	Gly	Glu	Glu	Glu	Ala	35	40	45	
Arg	Gln	Val	Ala	Ala	Glu	His	Gly	Phe	Gly	Val	Arg	Lys	Leu	Pro	50	55	60	
Phe	Ala	Glu	Gly	Leu	Tyr	His	Phe	Tyr	His	Asn	Gly	Leu	Ala	Lys	65	70	75	
Ala	Lys	Arg	Arg	Arg	Ser	Leu	His	His	Lys	Arg	Gln	Leu	Glu	Arg	80	85	90	
Asp	Pro	Arg	Ile	Lys	Met	Ala	Leu	Gln	Gln	Glu	Gly	Phe	Asp	Arg	95	100	105	
Lys	Lys	Arg	Gly	Tyr	Arg	Asp	Ile	Asn	Glu	Ile	Asp	Ile	Asn	Met	110	115	120	
Asn	Asp	Pro	Leu	Phe	Thr	Lys	Gln	Trp	Tyr	Leu	Phe	Asn	Thr	Gly	125	130	135	
Gln	Ala	Asp	Gly	Thr	Pro	Gly	Leu	Asp	Leu	Asn	Val	Ala	Glu	Ala	140	145	150	
Trp	Glu	Leu	Gly	Tyr	Thr	Gly	Lys	Gly	Val	Thr	Ile	Gly	Ile	Met	155	160	165	

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FIG. 4B

Asp	Asp	Gly	Ile	Asp	Tyr	Leu	His	Pro	Asp	Leu	Ala	Tyr	Asn	Tyr	180
									175						175
Asn	Ala	Asp	Ala	Ser	Tyr	Asp	Phe	Ser	Ser	Asn	Asp	Pro	Tyr	Pro	195
									185						190
Tyr	Pro	Arg	Tyr	Thr	Asp	Asp	Trp	Phe	Asn	Ser	His	Gly	Thr	Arg	210
									200						205
Cys	Ala	Gly	Glu	Val	Ser	Ala	Ala	Ala	Ser	Asn	Asn	Ile	Cys	Gly	225
									215						220
Val	Gly	Val	Ala	Tyr	Asn	Ser	Lys	Val	Ala	Gly	Ile	Arg	Met	Leu	240
									230						235
Asp	Gln	Pro	Phe	Met	Thr	Asp	Ile	Ile	Glu	Ala	Ser	Ser	Ile	Ser	255
									245						250
His	Met	Pro	Gln	Leu	Ile	Asp	Ile	Tyr	Ser	Ala	Ser	Trp	Gly	Pro	270
									260						265
Thr	Asp	Asn	Gly	Lys	Thr	Val	Asp	Gly	Pro	Arg	Glu	Leu	Thr	Leu	285
									275						280
Gln	Ala	Met	Ala	Asp	Gly	Val	Asn	Lys	Gly	Arg	Gly	Gly	Lys	Gly	300
									290						295
Ser	Ile	Tyr	Val	Trp	Ala	Ser	Gly	Asp	Gly	Gly	Ser	Tyr	Asp	Asp	315
									305						310
Cys	Asn	Cys	Asp	Gly	Tyr	Ala	Ser	Ser	Met	Trp	Thr	Ile	Ser	Ile	330
									320						325

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FIG. 4C

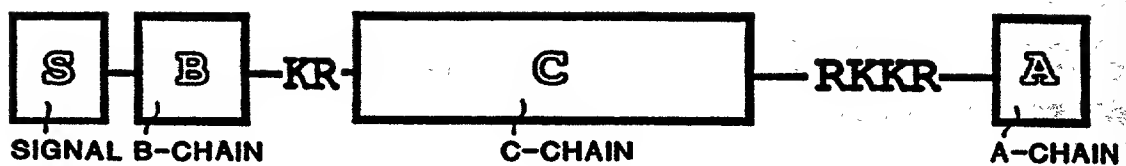
Asn Ser Ala Ile Asn Asp Gly Arg Thr Ala Leu Tyr Asp Glu Ser	335	340	345
Cys Ser Ser Thr Leu Ala Ser Thr Phe Ser Ser Asn Gly Arg Lys Arg	350	355	360
Asn Pro Glu Ala Gly Val Ala Thr Thr Asp Leu Tyr Gly Asn Cys	365	370	375
Thr Leu Arg His Ser Gly Thr Ser Ala Ala Ala Pro Glu Ala Ala	380	385	390
Gly Val Phe Ala Leu Ala Leu Glu Ala Asn Leu Asp Leu Thr Trp	395	400	405
Arg Asp Met Gln His Leu Thr Thr Val Leu Thr Ser Lys Arg Asn Gln	410	415	420
Leu His Asp Glu Val His Gln Trp Arg Arg Asn Gly Val Gly Leu	425	430	435
Glu Phe Asn His Leu Phe Gly Tyr Gly Val Leu Asp Ala Gly Ala	440	445	450
Met Val Lys Met, Ala Lys Asp Trp Lys Thr Val Pro Glu Arg Phe	455	460	465
His Cys Val Gly Gly Ser Val Gln Asn Pro Glu Lys Ile Pro Pro	470	475	480
Thr Gly Lys Leu Val Leu Thr Thr Lys Thr Asn Ala Cys Glu Gly	485	490	495

FIG. 4D

Lys Glu Asn Phe Val Arg Tyr Leu Glu His Val Gln Ala Val Ile 500 505 510
Thr Val Asn Ala Thr Arg Arg Gly Asp Leu Asn Ile Asn Met Thr 515 520 525
Ser Pro Met Gly Thr Lys Ser Ile Leu Leu Ser Arg Arg Pro Arg 530 535 540
Asp Asp Asp Ser Lys Val Gly Phe Asp Lys Trp Pro Phe Met Thr 545 550 555
Thr His Thr Trp Gly Glu Asp Ala Arg Gly Thr Trp Thr Leu Glu 560 565 570
Leu Gly Phe Val Gly Ser Ala Pro Gln Lys Gly Leu Leu Lys Glu 575 580 585
Trp Thr Leu Met Leu His Gly Thr Gln Ser Ala Pro Tyr Ile Asp 590 595 600
Gln Val Val Arg Asp Tyr Gln Ser Lys Leu Ala Met Ser Lys Lys 605 610 615
Gln Glu Leu Glu Glu Leu Asp Glu Ala Val Glu Arg Ser Leu 620 625 630
Gln Ser Ile Leu Arg Lys Asn 635 637

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FIG. 5



<u>Mutant</u>	<u>B/C-Chain</u>	<u>C/A-Chain</u>	<u>Processing</u>
Rx. wt	-KR-↓	-RKKR-↓	<p>H2RELAXIN</p>
Rx1	-KR-↓	-VKKR-↓	
Rx2	-KR-↓	-RAKR-↓	
Rx3	-KR-↓	-R↓KAR-	<p>H2RELAXIN</p>
Rx4	-KR-↓	-RKRR↓A-	
Rx7	-AR-	-RKKR-	<p>proH2RELAXIN</p>
Rx8	-KA-	-RKKR-	